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MEMORANDUM ON TETANUS.

(FOURTH EDITION.)

Issued by the War Office Committee for the Study of Tetanus.

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In March, 1916, the Director-General, Army Medical Service, appointed a Committee for the Study of Tetanus, and its prophylaxis. The present constitution of the Committee is as follows :—

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Major F. W. Andrewes, F.R.S., R.A.M.C. (T.).
Sir Kenneth Goadby, K.B.E., M.R.C.S.
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MEMORANDUM ON TETANUS.

(FOURTH EDITION.)

This Memorandum on the prophylaxis and treatment of tetanus has been drawn up with the authority of the War Office by the War Office Committee for the Study of Tetanus, and is to a great extent based on experimental and clinical evidence which has become available since the beginning of the war.

It is divided into the following sections :—

The Memorandum was first issued in August, 1916, a revised edition in October of the same year, and a third edition in June, 1917. Later progress in the study of tetanus necessitates a further revision of the Memorandum.

A question has arisen as to whether this Memorandum is to be looked upon as an Army Order or as a number of suggestions which may or may not be carried out, according to the inclination or judgment of the officers in charge of hospitals. In answer to this it may be stated that, in so far as it concerns the prophylactic or preventive treatment, the Memorandum should be regarded in the former sense ; and in so far as it concerns the therapeutic or curative treatment, in the latter sense. It has never been the policy of the Army Medical Authorities to interfere with the treatment of the sick soldier by his Medical Officer. With regard to prophylaxis, on the contrary, whether of small-pox, typhoid fever, or tetanus, it is an Army Order which must be carried out, whatever the personal predilections of the Medical Officers in charge of hospitals may be.

Throughout this Memorandum the word "unit" in relation to tetanus antitoxin means the official unit of the United States of America.

The United States of America unit of tetanus antitoxin was defined on October 25, 1907, in a circular issued by the Treasury Department, Washington, as follows :—

"The immunity unit for measuring the strength of tetanus antitoxin shall be ten times the least quantity of antitetanic serum necessary to save the life of a 350-gram guinea pig for 96 hours against the official test dose of a standard toxin furnished by the Hygienic Laboratory of the Public Health and Marine-Hospital Service . . . . The test dose is 100 minimal lethal doses of a precipitated toxin preserved under special conditions."

I.—PROPHYLACTIC OR PREVENTIVE TREATMENT OF TETANUS.

(*a*) General Surgical Prophylaxis.

Complete and early excision of gunshot wounds is a most potent factor in the prevention of tetanus. Only a small percentage of such wounds (certainly less than 3 per cent.) is found free from bacteria. Practically no lacerated shell wound heals by first intention without surgical intervention, whereas many such wounds excised within 12 hours of wounding, heal and recover as rapidly as a primary aseptic operation wound. Excised wounds which have broken down after primary suture, and non-excised wounds, usually contain both ærobic and anærobic bacteria, many of the latter end-sporing organisms. Even in the excised wounds which have failed to heal by first intention, the numbers and varieties of anærobic bacilli are strikingly less than in non-excised wounds.

Thus in 100 wounds subjected to immediate excision, 30 contained end-sporing bacteria, while in 100 non-excised wounds, 60 contained these anærobes, 30 against 60 per cent. The tetanus bacillus has been especially sought for in wounds of men showing no clinical signs of tetanus ; in 30 excised wounds virulent tetanus bacilli were demonstrated but once (3·3 per cent.), while in 70 non-excised wounds they were found 18 times (25·8 per cent.). Cases of tetanus are reported with incubation periods of many months, and exemplify latent tetanus infection.

Symbiosis between ærobic and anærobic bacteria is apparently of great importance in the initial stages of tetanus, gas-gangrene and other wound diseases, the growth of ærobic bacteria in damaged tissue promoting the development of anærobic organisms. Sequestra removed from wound areas three or four years after wounding have been found to contain end-sporing anærobic bacteria ; the majority of these sequestra show unaltered bony structure and were evidently detached at the time of the original injury. They are commonest in wound tissue which has been the seat of prolonged sepsis. Histological examination of these sequestra points to their origin from compact bone. The Haversian canals are frequently blocked with a coagulum containing entangled bacteria. Cultivations from the sinus leading to these sequestra often give ærobic cocci only, although the sequestrum and the granulation tissue removed from its bed give abundant anærobic growth. Metal fragments and bullets removed from completely healed wounds are by no means always sterile but in many instances give anærobic growths.

The surgical prevention of tetanus, therefore, consists of the free removal of all damaged tissues before the organisms carried into the wound have developed to a dangerous degree. This will probably be within the first twelve hours of wounding. In excising the wound area care should be taken that no incision is carried from infected wound tissue into surrounding healthy tissue, and instruments used to manipulate wound surfaces superficial and deep, should not be used on the surrounding healthy tissue ; clean cutting with a knife is better than scissors as less likely to leave bruised tissue behind. All metal fragments and other foreign bodies should be removed and careful search made for detached bone fragments, including those driven into the surrounding soft parts. The removal of large fragments must always be at the discretion of the surgeon, but it may be pointed out that the life of a fragment will partially depend upon the length of the period the fragment has been subjected to suppuration.

Instances are on record of local tetanus which has persisted until a sequestrum was removed or exfoliated. In local tetanus the removal of sequestra or foreign bodies in the vicinity of the wound disclosed by radiograms should be performed as routine treatment but only after a prophylactic injection of antitetanic serum. When removing the foreign body the fibrous capsule enclosing it should also be dissected away.

(*b.*) Serum Prophylaxis.

The prophylactic value of injections of antitetanic serum is beyond all doubt, but there is both clinical and experimental evidence that in about ten days the immunity conferred by an injection has already begun to fade and thenceforward steadily declines.

It is impossible, from the appearance of any wound, to determine whether it is infected with tetanus bacilli or not; and whereas many cases of tetanus have occurred not only in men with healed wounds, but also in those whose wounds were from the beginning apparently clean, it has been decided that all wounded men shall receive at least four injections of antitetanic serum, that is to say, a primary injection given at the time of the wound and three others.

The second, third and fourth subcutaneous injections must therefore be given to all wounded men. In order to anticipate the disappearance of antitoxin from the body, the second injection should follow the first at an interval of seven days, or as soon after this as possible. The third and fourth injections should also follow at as nearly as possible the same interval of time.

Cases of Trench Foot and Frost Bite, with or without obvious breach of surface, must be treated as wounded men.

If on account of the exigencies of war a second inoculation has not been given in France and on arrival in England it is found that a period of 15, 30 or more days has elapsed since the primary injection, the second, third and fourth should still be given.

Wounds received at home, for instance in aeroplane accidents, especially those which have been contaminated with soil, should be treated in the same way, as regards prophylactic injections, as gunshot wounds received overseas. Several cases of tetanus have also occurred in soldiers in England from trivial wounds, such as a scratch from barbed wire, or a wound from a fish bone when working on land treated with fish manure.

Care should therefore be taken in such cases, if there is any suspicion of dirt contamination, to ensure that the usual prophylactic dose of serum is given.

These multiple prophylactic inoculations have been in vogue more or less since the beginning of 1917. At present the number of our wounded who receive four inoculations is very various, depending on the energy of the local authority. It may be said to vary between 40 and 90 per cent. The main result of multiple inoculations should be the lowering of the incidence of tetanus among the wounded. There is no evidence at present as to whether this is so or not as the figures are not yet available. In regard to the lowering of the death-rate the following table gives all the information up to the present date: —

No. of Injections.	No. of Cases of Tetanus.	Recovered.	Died.	Mortality per cent.
1	201	157	44	21·9
2	166	133	33	19·8
3	65	53	12	18·5
4	43	39	4	9·3
5	15	14	1	6·6
6	2	2	—	—

The Tetanus Committee is of opinion that until our knowledge of the immunising process in tetanus is more advanced these multiple injections should be continued.

II.—DOSAGE IN PROPHYLACTIC OR PREVENTIVE TREATMENT OF TETANUS.

It may be definitely stated that the danger of anaphylactic shock is negligible when prophylactic doses of 500 U.S.A. units contained in 3 c.cm. or less of horse serum are given subcutaneously. This holds good however long the interval between the injections may be. There may be sometimes a serum rash. The primary injection, given at the front, has hitherto been 500 units, as recommended by the Tetanus Committee, and has proved as a rule an adequate prophylactic dose.*

The primary injection is given as a rule at the Dressing Station of a Field Ambulance, as soon as the wounded soldier is removed from the firing line. The second and following injections will most frequently be given at Home Hospitals, and sometimes injections will have to be given at Auxiliary Hospitals. The ordinary phial usually contains 1,500 units of tetanus antitoxin. Phials containing a single dose of 500 units are also now available. There is no necessity to sterilise the syringe after each injection, as the serum is aseptic, and, moreover, contains an antiseptic; it will be sufficient if a freshly sterilised needle be used for each case.

It is most important that every care should be taken to ensure that the skin, needle, and syringe are thoroughly sterile. Neglect of this precaution is very apt to lead to abscess formation.

These prophylactic injections may be given intramuscularly, and in the opinion of some, when given by this route there is less likelihood of abscess formation than when given subcutaneously.

If abscesses occur, which cannot be traced to faulty technique, the batch of serum should be withdrawn and samples in the form of unopened phials sent for bacteriological examination to the Officer in charge Vaccine Department, Royal Army Medical College, Grosvenor Road London, S.W. 1.

* In November, 1918, the dose was raised by the medical authorities in France to 1,500 units, in the hope that an even higher degree of immunity may be conferred. The second, third and fourth injections remain at 500 units.

III.—PRECAUTIONS TO BE TAKER BEFORE OPERATING ON WOUNDS.

It has repeatedly been observed that an attack of tetanus has followed operative interference with wounds, even when these have been long healed. In 1,000 cases of tetanus which have occurred in this country during the war, 72 or (7·2 per cent.) have appeared after operations. The explanation lies in the fact already mentioned that virulent tetanus bacilli, and also the bacilli of gas-gangrene, may persist in wounds for long periods. In one case tetanus bacilli were found as late as 882 days after the reception of the injury. Histologically these organisms are found encapsulated in fibrous tissue and thus protected from the action of the body fluids, but their vitality is unimpaired and they are quite capable of giving rise to tetanus if disturbed by subsequent surgical operations.

For these reasons it should be an invariable rule to give a precautionary dose of antitetanic serum (500 units) at the time of any operative measures at the site of a wound.

IV.—DIAGNOSIS.

The classical symptoms of tetanus, as described in the majority of the text-books, refer to a phase of the disease in which treatment has lost much of its power and value. With many medical men, tetanus is not tetanus until the symptoms of *risus sardonicus* and lockjaw are present.

In those who have been partially protected by a prophylactic injection of antitoxin, trismus and general symptoms may not occur at all, or not until late in the disease, possibly not until months have elapsed. This is known as delayed tetanus. In such cases the manifestations of tetanus may be confined to local spastic rigidity of the wounded limb, which may persist for weeks or months and then disappear; or may develop into generalised tetanus. This so-called localised tetanus is a distinct and not infrequent type of the disease and should be carefully watched for.

According to some clinicians there may be a local spasm of the muscles in the neighbourhood of a wound or scar not due to tetanus toxin. In such cases the greatest care should be taken before the diagnosis of localised tetanus is excluded, as a case of localised tetanus may become generalised even after the wound is healed.

There is also sometimes a difficulty in diagnosing between cases of localised tetanus, and cases which are purely functional. An intrathecal injection often clears up the diagnosis rapidly by suggesting to the patient the urgency of a rapid recovery.

The early diagnosis of tetanus is of the greatest importance. All clinical and experimental evidence tends to show that the earlier serum treatment is begun the greater the chance of success.

Tetanus toxin reaches the motor nerve cells of the central nervous system by travelling up the nerves; it is not directly conveyed to these cells by the blood. In a large number of cases the toxin appears to reach the spinal cord primarily by the nerves, which are

in connection with the seat of the injury, and, therefore, the motor nerve cells governing the muscles around the wound will be the earliest affected, such affection showing itself in the form of spasticity and increased reflex excitability of these muscles. The patient may complain of jerking or jumping, or stiffness in the affected limb, occurring especially at night. In some cases these symptoms may precede the other symptoms of tetanus by many hours or days. It is therefore desirable that the muscles in the vicinity of the wound should be examined whenever dressings are removed, and the occurrence of rigidity or twitchings, or of local increased reflex response to gentle tapping or pressure, should be immediately reported to the surgeon in charge.

All nursing sisters engaged in dressing wounds should be warned to give the alarm if the muscles round the wound are found to be harder or more rigid than the muscles of the uninjured limb or side.

Tetanus toxin is also absorbed from the wound into the blood stream and reaches the central nervous system by way of motor nerves other than those in direct anatomical continuity with the wound, and hence early symptoms may sometimes be observed in muscles supplied by any motor segment of the cord or brain.

The muscles supplied by the fifth nerve are those most commonly affected, as is shown by the occurrence of trismus as an early symptom.

Restriction of the lateral movement of the mandible should also be looked for.

Before concluding that trismus is due to tetanus, care should be exercised to exclude obvious local causes of the condition, such as alveolar abscess, especially in relation with the lower wisdom teeth.

In a wounded man this symptom should be taken as a decisive indication of tetanus in the absence of any other obvious source of reflex spasm. Other cranial nerve symptoms may be facial spasm or paralysis, or paralysis or spasm of the eye muscles with consequent strabismus.

Spasm of the pharyngeal muscles may also occur, which is often complained of by the patient as sore throat, and occasionally causes reflex yawning. The tongue muscles may be affected, causing deviation of the tongue when protruded. Tetanic spasm of the neck muscles may be complained of as stiff neck. Spasm of the thoracic and abdominal muscles is an occasional early symptom, often giving rise to complaints of stitch in the side or to difficulty in micturition.

Often before the onset of any definite symptom of tetanus there is a general increase of muscular tone, and the deep reflexes are exaggerated ; knee and ankle clonus may be produced in the absence of any signs pointing to the involvement of the pyramidal tract, such as an extensor plantar response or loss of the abdominal reflexes.

The general increase of tone is manifested in the facial muscles by the drawn expression of the patient, and the increased reflex excitability often leads to psychical irritability and insomnia.

The occurrence of a generalised tetanic toxæmia may be marked by profuse local or generalised sweating.

Constipation is an early symptom and is very obstinate as a rule.

Once the diagnosis of tetanus has been definitely established, the patient should be examined as little as possible.

It is very desirable to obtain the co-operation of medical officers in the endeavour of the Committee to formulate the early symptomatology of this disease, and therefore confimation of, or any addition to the above, will be welcomed.

Any brief account of early symptoms observed, either in the major or in the minor forms of the disease, will be of great value, and officers are requested to forward any such observations to Major-General Sir David Bruce, Chairman of the Tetanus Committee, at the Lister Institute, Chelsea Bridge Road, S.W. 1.

V.—CLASSIFICATION.

At the beginning of the war only the proportion of cases of generalised tetanus to cases of localised tetanus was recorded. Since June, 1917, a more detailed classification has been introduced. This has been based on the old systems, in order that a comparison between pre-serum and present-day results may be made easier. It would much help this if those in charge of cases would take great care to place each case in its right place on the blue form (A.F. W. 3508). This will also be found of some use as each type has its own death-rate. The following is the grouping at present in use :—

(A) Trismus the earliest symptom :—
   1. Complete closure of jaws (teeth cannot be separated) developing within 24 hours from onset.
   2. Complete closure of jaws developing after more than 24 hours.
   3. With incomplete closure of jaws. Mouth can be partially opened.

(B) Trismus occurring after other symptoms have shown themselves.

(C) General tetanus, without trismus.

(D) Local tetanus, without trismus.

VI.—THERAPEUTIC OR CURATIVE TREATMENT OF TETANUS.

It cannot be too strongly emphasised that time is the all-important element in the treatment of tetanus. As short a time as possible should be allowed to elapse between the diagnosis and the commencement of active treatment. A delay of an hour may make all the difference between success and failure.

It is on this account that the early symptoms are of the greatest importance. In almost every case of tetanus in those who have received a prophylactic dose of antitoxin there are found local manifestations of the disease, very often hardness and rigidity of

the muscles round the wound, and these signs can be seen or felt for days or even weeks before the occurrence of trismus. In a case on record, these local symptoms had been present for three weeks before the trismus showed itself and before tetanus was suspected. One medical officer is reported to have said that symptoms of tetanus were present in a case, but were not sufficiently severe to justify the use of antitoxin. According to present ideas it should no longer be permissible to wait for the occurrence of lockjaw before deciding that the case is tetanus; 5,000 units of antitoxic serum are of more avail at the very beginning, when the disease is still localised, than 50,000 when the symptoms have become general. The moment, then, that any local manifestations of tetanus is observed it is recommended to proceed at once to vigorous specific treatment.

The treatment of tetanus may be divided into specific and symptomatic.

1. Specific.—Specific treatment consists in the giving of tetanus antitoxin, which has the power of neutralising the tetanus toxin with which it comes in contact. The problem in treatment is to bring about this contact in the fullest and speediest manner. There are four methods which are commonly employed :—

(a) *Subcutaneous.*—In this method the serum is injected beneath the skin, from whence it is slowly absorbed into the circulation ; it has been determined that some 48 hours elapse before the maximum concentration in the blood is reached. This slowness of absorption is an advantage when it is desired that the action of the serum should be prolonged, as in prophylactic administration. But it is a grave disadvantage when quickness of action is all-important, as in acute tetanus ; in such a case little can be expected from this method at the beginning of treatment, although it is useful later in order to keep up the antitoxic action.

(b) *Intramuscular.*—Here the serum is injected into the muscles, from which it is absorbed into the circulation more rapidly than from the subcutaneous tissues. It is therefore, as regards speed, better than the subcutaneous method ; nevertheless, it must be remembered that full absorption, even here, takes 12 or more hours.

(c) *Intravenous.*—Here the serum is injected directly into the blood stream and immediately diffused throughout the body in such a way as to neutralise all circulating toxin. This is the most rapid route by which the neutralisation of circulating toxin can be accomplished. The objection to this method is that large doses of serum introduced into the circulation, especially in persons who have previously had an injection, is apt to bring about anaphylactic shock, which may prove fatal. Intravenous injection is therefore not recommended, except in cases where the intrathecal method is for any reason, impossible.

It may be added that the danger of anaphylactic shock may be diminished to a considerable extent by appropriate measures (*see* "Memorandum on the Use of Curative Sera").

Serum should not be given by the intravenous route unless the patient is anæsthetised, preferably with chloroform. During the progress of the injection the respiration should be carefully watched. Evidence of shock is provided by the fact that the breathing may become shallow and irregular. In more serious cases the respiratory movements entirely cease. The pulse may be increased in rate but may retain a good volume, even in cases where prolonged artificial respiration is necessary. Signs of shock usually make their appearance a few minutes after the serum has commenced to enter the vein. They may, however, be delayed until the time when anæsthesia is beginning to pass off. It is for this reason advantageous to continue the administration of the anæsthetic for 15 minutes after the completion of the injection.

(d) *Intrathecal.*—Here the serum is introduced by lumbar puncture into the sub-arachnoid space of the spinal canal. It soon begins to escape into the blood stream, so that the neutralisation of circulating toxin is quickly affected.

The Committee is of opinion that in acute general tetanus, the best method of treatment lies in the earliest possible administration of a large dose of antitoxic serum by the intrathecal route, repeated on the following day, combined with, and followed on succeeding days by, subcutaneous and intramuscular injections.

The introduction of the serum into the subarachnoid space always produces turbidity of the cerebro-spinal fluid. due to polymorphonuclear leucocytosis; this reaction is sometimes associated with transient symptoms of meningeal irritation, which need cause no alarm. With strict precautions the risk of septic infection is negligible.

(e) *Other routes.*—In some few cases the serum has been administered by the mouth, by the rectum, or as a local application to the wound itself. In one case 2,900,000 units were given by the rectum. As far as it is known these methods of giving antitoxin are quite useless and wasteful.

In the *chronic forms of tetanus*, particularly the form of localised tetanus limited to one limb, without trismus or other signs of generalisation, there appears to be no need to resort to intrathecal injection. A course of serum treatment by the subcutaneous or intramuscular method will, in most cases, do all that is required.

VII.—DOSAGE IN THE THERAPEUTIC OR CURATIVE TREATMENT OF TETANUS.

Experience has shown that in the treatment of acute general tetanus the best results are obtained from very large doses of serum; the more acute the case the larger should be the doses of serum employed. The object is to saturate the body with antitoxin as quickly as possible and to maintain the saturation. For this purpose from 50,000 to 100,000 units may be given during the first few days of treatment.

Tetanus antitoxin is issued to military hospitals in two strengths. The weaker is put up in phials containing either 500 or 1,500 units, the more concentrated in phials containing 8,000 units. Every general hospital should have in stock a supply of the high potency serum in order that there may be no delay should a case of acute tetanus occur in the district. This high potency serum should always be employed for intrathecal injections because this route differs from the others in the fact that the amount of fluid which can be introduced is limited. This high potency serum should be reserved for intrathecal injections alone.

The amount of cerebro-spinal fluid which can be withdrawn on lumbar puncture will not, as a rule, be more than 20 c.cm. It is usually held to be undesirable to run in more serum than will replace the cerebro-spinal fluid drawn off, and in cases when little or no fluid can be withdrawn it is not wise to inject more than 20 c.cm. of serum, *and this very slowly.* The 16,000 units contained in two phials of the high potency serum is an adequate single dose for intrathecal injection. It may be supplemented by intramuscular or subcutaneous injection.

When the disease shows distinct signs of abating the dose may be decreased, the interval between the doses lengthened and the serum given only subcutaneously.

The following outline of treatment may be suggested as an example of serum treatment in early acute tetanus :—

Day.	Sub-cutaneous.	Intra-muscular.	Intrathecal.
1st day	—	8,000	16,000
2nd day	—	8,000	16,000
3rd day	—	4,000	—
4th day	—	4,000	—
5th day	2,000	—	—
7th day	2,000	—	—
9th day	2,000	—	—

In local tetanus, without implication of the higher centres, doses of 3,000 to 6,000 units may be given every second or third day by the intramuscular or subcutaneous routes. But if in such cases the disease shows signs of extending to the higher centres, it is recommended to give at least one full dose by the intrathecal route.

Symptomatic.—Symptomatic treatment consists in the exhibition of sedative drugs. Morphia may be given in $\frac{1}{4}$-grain doses and administered every four hours—some prefer full doses of chloral hydrate ; potassium bromide, chloretone, or paraldehyde may also be given by the mouth or rectum.

Carbolic acid.—There is no convincing evidence that the carbolic acid treatment of tetanus has any curative effect whatever, or any action upon the course of the disease. It is not recommended.

Magnesium sulphate.—Treatment by sulphate of magnesium has no effect upon the disease itself. The cessation of spasm which follows an injection is only temporary, and is purchased at the cost of risks which are far from negligible.

VIII.—ANAPHYLAXIS.

The War Office has issued a "Memorandum on the Use of Curative Sera" which discusses anaphylactic shock, its causes and treatment. This Memorandum should be consulted by medical officers before treating cases of tetanus. Copies can be obtained from the D.D.M.S. in the different Commands or from A.M.D. 2, War Office.

Anaphylactic Shock after Prophylactic Injections.

Serious symptoms resulting from a small subcutaneous injection of serum are exceedingly rare, but very occasionally severe shock may follow the administration of the customary small prophylactic dose of 500 units. In such cases a history of symptoms following previous prophylactic injections may sometimes be obtained. In severe cases signs of collapse may occur within a few minutes or may be delayed for several hours. There is extreme weakness and prostration and the patient is acutely alarmed. Respiration becomes shallow and irregular and the pulse is rapid and small in volume. There may be urticaria and in some cases œdema of the eyelids, palate, and other parts of the body. Recovery may be complete within an hour. In other cases the patients remain in a weak and collapsed state for many hours, during which period the respiratory movements remain shallow and the pulse may be rapid, of poor volume and sometimes irregular.

In England alone, during the war it is probable that some two millions of prophylactic doses of antitetanic serum have been given. Out of this huge number only eleven cases of shock have been reported. All eleven cases recovered. The history of these cases is usually given as follows: "two minutes after the injection there was severe collapse, pulse feeble, the patient thought he would die." In another case "severe rigor, shaking and profound collapse, cyanosed and pulseless, expected to die, acute symptoms passed off within two hours." No doubt these cases appear very alarming, but they are so rare that the Committee are justified in stating "that the danger of anaphylactic shock is negligible when prophylactic doses of 500 units contained in 3 c.cm. or less of horse serum are given subcutaneously."

Anaphylactic Shock Following the Therapeutic Use of Serum.

Since the beginning of the war nearly 1,400 cases of tetanus have been reported as having occurred in wounded soldiers under

treatment in England. Forty-nine cases of shock have been notified (3·5 per cent.). There were 12 deaths (0·8 per cent.). Fifteen cases were reported as severe, 6 as moderate, and 16 as mild.

Of the 49 cases of shock, 17 were caused by intrathecal injections, 14 by intravenous, 9 by intramuscular, and 2 by subcutaneous, In 7 it is doubtful which injection caused the shock. Of the whole number of cases of tetanus, 757 received intrathecal, 232 intravenous, 736 intramuscular, and 819 subcutaneous injections. It follows then that 2 per cent. of the cases of shock followed the intrathecal injection, 6 per cent. after intravenous, 1·2 per cent. after intramuscular, and 0·2 per cent. after subcutaneous injections. It is evident from these figures that the most dangerous route for the therapeutic injection of antitetanic serum is the intravenous, and that the Tetanus Committee were justified in not recommending it.

In the descriptions of shock the following symptoms are prominent. The skin and mucous membranes are pale. There may be profuse sweating. The eyelids often become œdematous and subcutaneous œdema may be observed in other parts of the body. In some cases an urticarial rash appears which may subside in a few minutes, or may persist for hours or days. The respirations become shallow or irregular or cease altogether. The marked feature of anaphylactic shock is an extreme fall in the blood pressure, the pulse becomes imperceptible and the body cyanosed.

IX.—SURGICAL TREATMENT OF THE WOUND AFTER TETANUS HAS APPEARED.

There was formerly a general impression that it is of advantage to amputate the limb, or excise the wound, as a means of arresting acute general tetanus. Animal experiments, however, suggest that operative treatment is of no avail as a curative measure.

The experience gained during the war suggests that amputation is of little service in acute tetanus and may actually hasten a fatal issue ; where, however, in subacute or chronic cases the wound is foul, operative measures are often of advantage and especially the removal of foreign bodies or sequestra. This should never be done without the previous administration of antitoxin.

X.—TYPES OF TETANUS BACILLI.

Investigation undertaken on behalf of the Tetanus Committee has shown that there are at least four varieties of the tetanus bacilli. These varieties or "types" have been differentiated from one another by serological tests.

Of 100 strains obtained from cases of the disease, 41 qualified as Type I bacilli, 22 as Type II, 33 as Type III, and 4 as Type IV.

The majority of the men from whose wounds these bacilli were obtained had received antitetanic serum prophylactically. The death rates from the infections due to the various types were as follows:—Type I, 10 per cent. ; Type II, 28 per cent. ; Type III, 35 per cent.

The tetanus bacillus can also be recovered not infrequently from wounds of men who show no symptoms of the disease. In one series of 100 wounds it was found in 19 instances. Of these 19 strains obtained from such "indifferent" wounds, 15 (75 per cent, qualified as Type I bacilli, 2 as Type II, 1 as Type III, and 1 as Type IV.

These figures suggest that Type I is less virulent than Types II and III or that the serum at present in use confers more adequate protection against infection due to Type I than against that due to Type II or Type III.

The number of cases so far successfully investigated is much too small to permit of an opinion being offered concerning the validity of either of these hypotheses. It is desirable then that as many cases as possible be examined bacteriologically as the "type" of the bacillus responsible for the causation of tetanus may prove of some importance in its pathology and therefore in its serum prophylaxis and serum therapeutics.

XI.—THE ADDITION TO THE ANTITETANIC SERUM OF THE ANTITOXINS OF OTHER ANÆROBES FOUND IN WOUNDS.

The Tetanus Committee think it desirable to record here, for the sake of the future student of tetanus, the attempts lately made to add to the tetanus antitoxin, the antitoxins of other anærobes infecting wounds. It may be said at the onset that no satisfactory or practical results came of these attempts, since the war suddenly ended when the experiments were hardly under way.

It is only since the outbreak of the present war that the importance of gas-gangrene as a dangerous and fatal complication of gunshot wounds, and as an active aider and abettor of the tetanus bacillus, has been justly estimated. In January, 1918, Major Bull, U.S.A., gave a demonstration at the Royal Army Medical College on the production of toxin by *Bacillus welchii*, one of the principal gas-gangrene organisms. Shortly after this, and arising out of it, the Tetanus Committee recommended that a serum containing the antitoxin of *B. welchii*, in addition to that of the tetanus bacilli, should be prepared if possible and put into use as a prophylactic in place of the simple tetanus antitoxin hitherto in use. Dr. R. A. O'Brien, a member of the Tetanus Committee, had in the meantime been preparing a quantity of the antitoxin.

In the summer of 1918 an experiment was made in France under the auspices of the Medical Research Committee to determine the value of this double serum. Certain army areas were chosen, and the double serum issued to alternate Field Ambulances in those areas. The remaining Field Ambulances received the ordinary antitetanus serum. At the same time, instructions were issued to provide for the recording on each wounded man's Field Medical Card the kind of serum he received, A.T.S. or A.T.S.+W.

The result of the experiment showed that the addition of *B. welchii* antitoxin to the tetanus antitoxin had no effect in reducing the number of cases of gas-gangrene. This was probably due to the fact that the antitoxin prepared from the toxin of *B. welchii* was not powerful enough. There was no evidence that the addition had any effect, good or bad, on the tetanus antitoxin.

At a War Office conference, held on November 1, 1918, it was decided to add the antitoxins of *Vibrion Septique* and *B. œdematiens*, as well as the antitoxin of *B. welchii* to the tetanus antitoxin, and to replace the simple tetanus antitoxin by this new serum for general use in France. As it would be impossible, at least at first, to get a sufficiently large number of units of these different antitoxins into the 3 c.cm. of antitetanic serum hitherto in use, it was decided to increase the primary dose, if necessary, to 20 c.cm. of serum. The Tetanus Committee viewed with grave concern the contemplated increase in the quantity of serum necessitated by the use of a low potency gas-gangrene serum, and regarded with misgiving the possibility of general dissatisfaction arising towards tetanus prophylaxis should serum rashes frequently result from routine prophylactic injections of the quadruple serum.

XII.—SUPPLY OF ANTITETANIC SERUM OR ANTITOXIN.

The country generally has been divided into areas of about 10 miles radius, in each of which areas a central hospital acts as a distributing centre for serum so that it can issue to any of the hospitals in its area, without any delay, a sufficient supply of serum to begin the treatment of a case of tetanus.

The distributing centre indents on the general hospital of its Command for adequate supplies of serum for prophylactic and curative purposes. Serum should be stored in as cool a place as possible.

The quantity, not the quality, of antitoxin present in a serum gradually diminishes from the time the serum is collected. The rate at which this decrease takes place is more rapid when the serum is fresh than when it is older. After a time the serum may reach a condition of comparative stability. As the loss of antitoxin increases with rise of temperature, and as exposure to bright light has also a bad effect, serum should always be stored in the dark and in the cold. As regards the keeping quality of antitoxin in the tropics, there is no special reason why, if serum is properly stored, it should not keep well.

In the dry state, antitoxin is much less affected by heat, and dry antitoxin has been found to retain its potency for years practically unchanged. The disadvantage of dry powdered antitoxin is that it is extremely difficult to prevent contamination during the process of preparation.

In Appendix B will be found the official instructions with regard to the use of time-expired serum.

XIII.—INSTRUCTIONS TO INSPECTORS OF TETANUS.

In every Command one or more officers with special knowledge should be detailed by the D.D.M.S. to visit cases of tetanus and to assist when necessary in their treatment. These officers should be at the general hospitals of the district, and their names and telephonic addresses should be communicated to the officers and medical practitioners in charge of auxiliary and V.A.D. hospitals.

The working out of a scheme for the supply of serum and syringes to these subsidiary hospitals is a duty which devolves on the Inspector of Tetanus.

On the occurrence of a case of tetanus, the Inspector will be immediately informed, and he will at once proceed to visit the case and offer assistance in the carrying out of such treatment as has been suggested in the present Memorandum.

He will, if necessary, assist in the operation of lumbar puncture and intrathecal injection. This will seldom be necessary, as from what has already been said as to the danger of even an hour's delay, this intrathecal injection will usually have been given before his arrival.

He will make careful inquiry into the case in order to ascertain if any early symptoms had been present and had escaped notice. He will note what prophylactic injections have been made, and if omitted, will ascertain why they were omitted.

When visiting the hospital where the case has occurred he will ascertain if the other wounded men are receiving prophylactic injections.

He should see that sufficient notes of the case are being kept in order that the Tetanus Form can be filled up as fully as possible. For example, it is very seldom that the distinguishing marks on the bottles of serum are reported. This should be done because if serum trouble arises it is evident that this information is essential.

He will forward an Inspector's Report to Major-General Sir David Bruce with as little delay as possible.

The ordinary Tetanus Report, A.F. W. 3508, will be filled in by the medical officer in charge of the case. Too great care cannot be taken in this matter of the reports, as the value of any analysis made from them depends on their accuracy and completeness.

XIV.—INSTRUCTIONS TO OFFICERS IN CHARGE OF HOSPITALS.

Officers in charge of hospitals will be responsible for the administration of the second, third, and fourth prophylactic doses of antitoxin to all wounded under their care, unless grave reasons exist for withholding them. The administration of antitoxin will be recorded on the soldier's Field Medical Card, A.F. W. 3118.

The officer in charge of a hospital will satisfy himself that each medical officer in his hospital has a copy of the "Memorandum on

Tetanus" and that each sister, nurse or dresser of wounds has a copy of the "Notes on the Nursing of Tetanus." He will impress upon medical officers and nurses the paramount importance of early detection of symptoms and early specific treatment.

He will satisfy himself that the proper instruments and an adequate supply of antitoxin are ready to hand or within easy reach, in order that no delay may take place in beginning treatment. As soon as a case of tetanus is reported to him he will immediately inform the Inspector of Tetanus by messenger, telephone or telegram.

When patients are transferred from one hospital to another the number of injections given, with dates, must be entered on their Field Medical Cards.

This is the best document on which to record the prophylactic injections. It comes with the wounded soldier from overseas and accompanies him wherever he goes, as long as he remains in any hospital, that is, until he is discharged to duty or is invalided out of the service. By this means a complete history of his prophylactic serum treatment will be available in case the wounded man develops tetanus, and it will be possible in time to estimate the effect of the second, third and fourth injections.

Medical officers in charge of hospitals will, as heretofore, inform Major-General Sir David Bruce, by telegram, of the occurrence of a case of tetanus, giving the number, name, rank, and regiment, and on the recovery or death of the case forward the usual tetanus report to him, in accordance with War Office instructions. If the case recovers, this report, A.F. W. 3508, should be sent in as soon as the tetanus symptoms have subsided; it should not be kept back until the patient's discharge from hospital, as is often the case.

Any abnormalities of behaviour of antitetanic serum should be carefully observed and reported.

As the Tetanus Committee was appointed for the purpose of studying tetanus, it is greatly to be desired that every medical officer will co-operate in a collective investigation and submit any evidence in his possession which may add to our knowledge of the disease and its treatment.

XV.—INSTRUCTIONS TO MEDICAL OFFICERS IN CHARGE OF WOUNDED.

Every medical officer in charge of wounded will make himself acquainted with the contents of the Memorandum on Tetanus, No. 4779, A.M.D. 2, issued by the War Office, and will see that every nurse under him has a copy of the "Notes on the Nursing of Tetanus" also issued by the War Office, and will satisfy himself that she is fully aware of the importance of reporting early symptoms to the nearest available medical officer.

He will be responsible for the carrying out of the recommendations of the Tetanus Committee in regard to the prophylactic

injection of all wounded under his care, bearing in mind that cases of trench feet are especially dangerous.

Information regarding previous prophylactic injections will be obtained from the soldier's Field Medical Card, A.F. W. 3118.

As soon as tetanus is suspected, he will at once take steps to have the patient removed to a special ward, where light and sound can be excluded, and placed under the care of a thoroughly trustworthy and sympathetic sister.

The importance of such nursing details, as the protection of the patient from every kind of external stimulus, cannot be too strongly emphasised.

He will report the case to the medical officer in charge of the hospital. If the tetanus is generalised as shown by trismus and other symptoms, he should proceed at once to carry out serum treatment in accordance with the recommendations given in the section on curative treatment, without waiting for the Tetanus Inspector.

He is especially requested to keep careful notes on the case sheet of the symptoms and progress of the case in order that as full and complete a report as possible may be rendered on A.F. W. 3508.

XVI.—APPENDIX A.

The Method of Performing an Intrathecal Injection.

The patient should preferably be under general anæsthesia. The skin over the area of the fourth and fifth lumbar spines should be painted with iodine or cleansed with soap and water followed by an antiseptic. A spinal needle and syringe, or, if the gravity method be used, the usual india-rubber tubing, should be boiled in normal saline, and *the surgeon must observe throughout the most rigorous aseptic precautions.*

The patient is bent head to knees, so as to present as fully a curved back to the operator as possible, and the position of the fourth lumbar spine ascertained by drawing an imaginary line between the highest points of the crests of the ilia.

The tip of the finger is placed on the supraspinous ligament connecting the summits of the spinous processes of the fourth and fifth lumbar vertebræ. The needle is inserted about $\frac{3}{8}$ of an inch to one side of the middle line and directed forwards and slightly upwards and inwards. If the needle strikes the bone it should be withdrawn and a fresh attempt made. The canal is reached at a depth on an average of about $2\frac{1}{2}$ inches. The trochar is withdrawn and about 20 c.cm. of cerebro-spinal fluid allowed to flow out into a measured vessel. The syringe is then fitted to the needle and the serum injected. Many surgeons prefer to run in the serum by gravity, and this is undoubtedly a good method.

It is important that the serum be heated to the temperature of the body and that the injection be made very slowly.

The canal can also be reached by pushing the needle through the supraspinous ligament in the middle line halfway between the two spinous processes.

If several injections have to be made it is well to choose fresh sites.

Blocking of the flow of the cerebro-spinal fluid by a blood clot may be overcome by reinserting and withdrawing the trochar.

The bed should be tilted at the foot and the pillow removed for an hour or two after the injections.

XVII.—APPENDIX B.

Instructions with regard to the use of Time-Expired Antitetanic Serum.

On the 1st August, 1918, the War Office issued a Memorandum (24/Remedies/266 (A.M.D. 3)) concerning the period of use of sera and vaccines. The instructions regarding antitetanic serum are as follows :—

(*a*) For 12 months after the date of expiry add 10 per cent. to the dose.

(*b*) From 12 months to 18 months after the date of expiry add 20 per cent. to the dose.

(*c*) From 18 months to two years after the date of expiry add 30 per cent. to the dose.

(*d*) No serum to be used after two years after date of expiry without reference to this office.

XVIII.—APPENDIX C.

List of papers written by members of the Tetanus Committee and others, which may be consulted.

"Memorandum on the Use of Curative Sera." Issued by A.M.D. 2, War Office, 1917.

"Notes on the Nursing of Tetanus." Issued by A.M.D. 2, War Office, 1917.

"On the Intrathecal Route for the Administration of Tetanus Antitoxin." By Major F. W. Andrewes. *The Lancet*, May 5, 1917.

"Tetanus Relapse after a Trivial Operation." By Captain Stanley Barnes, R.A.M.C. *British Medical Journal*, March 17, 1917.

"An Analysis of Cases of Tetanus treated in Home Military Hospitals from August, 1914, to August, 1915." By Major-General Sir David Bruce. *The Lancet*, October 23, 1915.

"2nd Analysis of Cases of Tetanus treated in Home Military Hospitals from August 1, 1915, to July 31, 1916." By Major-General Sir David Bruce. *The Lancet*, December 2, 1916.

3rd Analysis of Cases of Tetanus treated in Home Military Hospitals from August to October, 1916." *The Lancet*, June 30, 1917. By Major-General Sir David Bruce.

"4th Analysis of Cases of Tetanus treated in Home Military Hospitals from October to December, 1916. By Major-General Sir David Bruce. *The Lancet*, December 15, 1917.

"5th Analysis of Cases of Tetanus treated in Home Military Hospitals from December, 1916, to March, 1917." By Major-General Sir David Bruce. *The Lancet*, December 22, 1917.

"6th Analysis of Cases of Tetanus treated in Home Military Hospitals from March to June, 1917." By Major-General Sir David Bruce. *British Medical Journal* (Summary only), March 16, 1918.

"7th, 8th, and 9th Analyses of Cases of Tetanus treated in Home Military Hospitals from June, 1917, to April, 1918." By Major-General Sir David Bruce. *British Medical Journal* (Summary only), October 12, 1918.

"Tetanus in Home Military Hospitals—Analysis of 1,000 cases." By Major-General Sir David Bruce. *Transactions of the Society of Tropical Medicine and Hygiene*, November, 1917.

"Note on the Incidence of Tetanus among Wounded Soldiers." By Major-General Sir David Bruce. *British Medical Journal*, January 27, 1917.

"Importance of Early Prophylactic Injection in Trench Foot." By Major-General Sir David Bruce. *British Medical Journal*, January 13, 1917.

"Intramuscular *versus* the Intrathecal route in the Treatment of Tetanus by the Injection of Antitoxin." By Major-General Sir David Bruce. *The Lancet*, May 5, 1917.

"Tetanus." By Major-General Sir David Bruce. *War Medicine*, December, 1918.

"An Analysis of Cases of Tetanus occurring in the British Armies in France between November 1, 1916, and December 31, 1917." By Colonel S. L. Cummins, C.M.G., A.M.S., and Major H. Graeme Gibson, R.A.M.C. *The Lancet*, March 1, 1919.

"Report on Twenty-Five cases of Tetanus." By Major H. R. Dean. *The Lancet*, May 5, 1917.

"Delayed Tetanus in Connection with Fractures." By Capt. M. Foster, R.A.M.C. (T.). *British Medical Journal*, February 2, 1917.

"A Note on the Reflexes in Tetanus." By Maj. A. G. Gibson, R.A.M.C. *The Lancet*, September 15, 1917.

"A Report on the Injection of Antitetanus Serum in Tetanus Cases." By Sir K. Goadby, M.R.C.S., L.R.C.P., D.P.H. Cantab. *R.A.M.C. Journal*, October, 1915.

"The Bacterial Flora of War Wounds." *British Medical Journal*, May 25, 1918. By Sir K. Goadby, K.B.E.

"A Comparison of Subcutaneous with Intravenous and Intrathecal Administration of Tetanus Antitoxin in Experimental Tetanus." By Capt. F. Golla, R.A.M.C. (T.). *The Lancet*, May 5, 1917.

"Analysis of Recent Tetanus Statistics." By Capt. F. Golla, R.A.M.C. *The Lancet*, February 29, 1918.

"Tetanus: its Prevention and Treatment by means of Anti-tetanic Serum." By Dr. A. T. MacConkey. *British Medical Journal*, October 10, 1914.

"The Prophylaxis of Tetanus: A Summary." By Dr A. T. MacConkey. *British Medical Journal*, December 11, 1915.

"Iodine in Tetanus." By Dr. A. T. MacConkey and S. S. Zilva. *British Medical Journal*, March 18, 1916.

"On the Passive Immunity Conferred by a Prophylactic Dose of Antitetanic Serum." By Dr. A. T. MacConkey and Annie Homer. *The Lancet*, February 17, 1917.

"A Plea for a Collective Study of Tetanus." By Dr. A. T. MacConkey. *R.A.M.C. Journal*, March, 1916.

"Keeping Qualities of Therapeutic Serum." By Dr. A. T. MacConkey. *British Medical Journal*, January 6, 1917.

"Observations with Antitetanus Serum in the Monkey." By Professor Sherrington, F.R.S. *The Lancet*, December 29. 1917.

"An Analysis of Recent Cases of Tetanus in the B.E.F." By Colonel Sir W. B. Leishman and Major A. B. Smallman. *The Lancet*, January 27, 1917.

"Concomitant Anærobic Injections in Tetanus." By Capt. W. J. Tulloch, R.A.M.C. *British Medical Journal*, June 1, 1918.

"The Isolation and Serological Differentiation of *B. Tetani*." By Capt. W. J. Tulloch, R.A.M.C. *Proceedings of the Royal Society*, Series B, April, 1918.

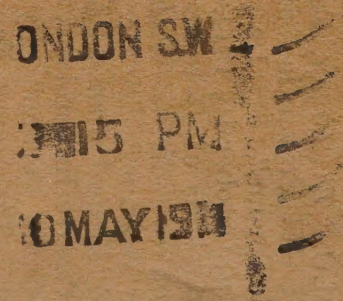
"The Distribution of the Serological Types of *B. tetani* in wounds of Men who received Prophylactic Inoculation and a Study of the Mechanism of Infection in and Immunity from Tetanus." By Brevet Major W. J. Tulloch, R.A.M.C. *Proceedings*, Royal Society, Series B (in the Press).

"Report on Bacteriological Investigations undertaken on Behalf of the War Office Committee for the Study of Tetanus." By Brevet Major W. J. Tulloch, R.A.M.C. *Journal of Hygiene* (in the Press).

"A Modern View of Tetanus." By Dr. F. Ransom. *The Lancet*, December 22, 1917.

"Observations on a Severe Case of Tetanus treated with Repeated Intrathecal Injections of Antitoxin." By Capt. C. C. Worster-Drought, R.A.M.C. *R.A.M.C. Journal*, January, 1918.

"A Case Illustrating an Extreme Modification of Local Tetanus." By Capt. C. C. Worster-Drought, R.A.M.C. *The Lancet*, June 1, 1918.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